UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,981	01/23/2004	Gyula Vigh	105-1-007	7892

27469 7590 09/06/2007

MALLINCKRODT & MALLINCKRODT
P.O. BOX 1219
SANDY, UT 84091-1219

EXAMINER	
VATHYAM, SUREKHA	
ART UNIT	**PAPER NUMBER**
1753	

MAIL DATE	DELIVERY MODE
09/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/763,981	VIGH, GYULA	
	Examiner	Art Unit	
	Surekha Vathyam	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 January 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Drawings

1. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: 33, 40 and 44 (in fig. 3).

2. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(4) because reference character "60" has been used to designate both section of auxiliary compartment occupied by auxiliary agent and pH gradient formed in the separation capillary.

3. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

4. The disclosure is objected to because of the following informalities: page 17, paragraph [0043], line 3, "DNS-Trp" should be changed to - -DNS-GABA- -.

Appropriate correction is required.

5. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: claims 16, 18, 19 and 31 – 34.

6. Claims 24 and 35 are objected to because of the following informalities: line 3 of claim 24 should be corrected to end in a period and not a semi-colon. In each of lines 9 and 13 of claim 35, line 6 of claim 36 and line 14 of claim 37, "amphlytes" should be corrected to - -ampholytes- -. Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 22 – 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

had possession of the claimed invention. Each of independent apparatus claims 22 and 23 recite the following limitations:

"a means of filling the anode compartment with an acidic solution and the cathode compartment with a basic solution".

"a means of filling the rest of the compartments with a solution that contains an ampholytic analyte".

"a means of applying a separation potential to the anode and the cathode".

Claim 23 additionally recites the limitation, "a means of adjusting in the ampholytic analyte containing solution the first amount of the one or more components selected from the group comprising a mixture of carrier ampholytes, strong electrolyte auxiliary agents, weak electrolyte auxiliary agents, and ampholytic auxiliary agents to a second amount".

Each of these means-plus-function claim limitations does not have corresponding structures described in the specification thereby failing to comply with the written description requirement.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 22 – 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. Each of independent apparatus claims 22 and 23 have the following limitations:

"a means of filling the anode compartment with an acidic solution and the cathode compartment with a basic solution".

"a means of filling the rest of the compartments with a solution that contains an ampholytic analyte".

"a means of applying a separation potential to the anode and the cathode".

Claim 23 additionally recites the limitation, "a means of adjusting in the ampholytic analyte containing solution the first amount of the one or more components selected from the group comprising a mixture of carrier ampholytes, strong electrolyte auxiliary agents, weak electrolyte auxiliary agents, and ampholytic auxiliary agents to a second amount".

Each of claims 22 and 23 is indefinite because the specification does not disclose a corresponding structure of a means-plus-function limitation. "If one employs means plus function language in a claim, one must set forth in the specification an adequate disclosure showing what is meant by that language. If an applicant fails to set forth an adequate disclosure, the applicant has in effect failed to particularly point out and distinctly claim the invention as required by the second paragraph of section 112." *In re Donaldson Co.*, 16 F.3d 1189, 1195, 29 USPQ2d 1845, 1850 (Fed. Cir. 1994) (in banc)

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1, 3 – 4, 7 – 23, 25 – 31, 33 and 35 – 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Vigh et al. (US 2002/0043465).

Regarding claim 1, Vigh ('465) discloses a method of improving a concentration detection limit for an ampholytic analyte in an isoelectric focusing system ([0057]) comprising the steps of: providing an isoelectric focusing system (see fig. 2) having a separation compartment (26, 28) disposed between an anode compartment (22, 24) and a cathode compartment (24, 22); providing a solution containing an ampholytic analyte ([0002], [0129]) and a mixture of carrier ampholytes ([0130]); providing at least one of the options selected from the group consisting of option one and option two, wherein option one uses one or more auxiliary compartments (28, 26) disposed between at least one of the anode compartment (22, 24) and the separation compartment (26, 28) or the cathode compartment (24, 22) and the separation compartment (26, 28), and option two uses one or more auxiliary agents mixed with the solution containing the ampholytic sample component; filling the anode compartment with an acidic solution and the cathode compartment with a basic solution ([0129]); filling the other compartments with the solution containing the ampholytic analyte ([0129]); applying a potential between an anode (88a, 88b) located in the anode

compartment and a cathode (88b, 88a) located in the cathode compartment ([0098] – [0099] and [0129]) and effecting an isoelectric focusing of the ampholytic analyte into the separation compartment ([0037] and [0099]); and detecting the focused ampholytic analyte in the separation compartment at its increased concentration over that provided by isoelectric focusing without the use of option one or option two ([0130]).

Regarding claims 3 and 4, Vigh ('465) discloses the method according to claim 1, wherein the isoelectric focusing system is an imaging capillary isoelectric focusing system ([0130]).

Regarding claims 7 and 8, Vigh ('465) discloses the method according to claim 1, wherein the auxiliary compartment (28, 26) and the adjacent electrode compartment (24, 22) are separated by an anti-convective, ion-permeable barrier (30, 32) such as a membrane that substantially eliminates convective mixing between the contents of the auxiliary compartment and the adjacent electrode compartment ([102], [106] – [107], [0115] – [0117]).

Regarding claims 9 – 19, Vigh ('465) discloses the method according to claim 1, option one, which uses one or more auxiliary compartments. Claim 1 requires only one of the alternatives, option one or option two. Because Vigh ('465) discloses option one and claims 9 – 19 further limit option 2, claims 9 – 19 are also anticipated by Vigh ('465).

Regarding claim 20, Vigh ('465) discloses the method according to claim 1, wherein one or more solubilizer selected from a group consisting of non-electrolytes and

zwitterions is additionally added to the sample solution to increase the solubility of the ampholytic analyte ([0090], [0092], [129], [0130]).

Regarding claim 21, Vigh ('465) discloses the method according to claim 1 wherein one or more complexing agent selected from group consisting of non-electrolytes and zwitterions is additionally added to the sample solution to improve the isoelectric focusing separation of the ampholytic analyte ([0090], [0092], [129], [0130]).

Regarding claim 22, Vigh ('465) discloses an apparatus (see fig. 1) comprising: a separation compartment (26, 28) disposed between an anode compartment (22, 24) and a cathode compartment (24, 22); an anode (88a, 88b) disposed in the anode compartment and a cathode (88b, 88a) disposed in the cathode compartment; one or more auxiliary compartments (28, 26) disposed between the anode compartment (22, 24) and the separation compartment (26, 28) or the cathode compartment (24, 22) and the separation compartment (26, 28); a means (40, 41) of filling the anode compartment with an acidic solution and the cathode compartment with a basic solution ([0087] – [0088], [0129]); a means (48, 58) of filling the rest of the compartments with a solution that contains an ampholytic analyte ([0089], [0091], [00129]), and one or more components selected from a group comprising a mixture of carrier ampholytes, strong electrolyte auxiliary agents, weak electrolyte auxiliary agents, and ampholytic auxiliary agents ([0090], [0092], [0130]); a means (72) of applying a separation potential to the anode and the cathode and effecting an isoelectric focusing of the ampholytic analyte into the separation compartment ([0098]); and a means of detecting the focused

ampholytic analyte in the separation compartment at its increased concentration over that provided by isoelectric focusing without the use of any auxiliary compartment and auxiliary agent ([0130]).

Regarding claim 23, Vigh ('465) discloses an apparatus (see fig. 1) comprising: a separation compartment (26, 28) disposed between an anode compartment (22, 24) and a cathode compartment (24, 22); an anode (88a, 88b) disposed in the anode compartment and a cathode (88b, 88a) disposed in the cathode compartment; one or more auxiliary compartments (28, 26) disposed between the anode compartment (22, 24) and the separation compartment (26, 28) or the cathode compartment (24, 22) and the separation compartment (26, 28); a means (40, 41) of filling the anode compartment with an acidic solution and the cathode compartment with a basic solution ([0087] – [0088], [0129]); a means (48, 58) of filling the rest of the compartments with a solution that contains an ampholytic analyte present in a salt-laden sample ([0039] – [0040], [0089], [0091], [00129]) and a first amount of one or more components selected from a group comprising a mixture of carrier ampholytes, strong electrolyte auxiliary agents, weak electrolyte auxiliary agents, and ampholytic auxiliary agents ([0090], [0092], [0130]); a means (72) of applying a separation potential to the anode and the cathode and effecting a first isoelectric focusing of the ampholytic analyte into the separation compartment ([0098]); a means of detecting at a first focusing position in the separation compartment the focused ampholytic analyte at its increased concentration ([0130]); a means of adjusting in the ampholytic analyte containing solution the first amount of the

one or more components selected from the group comprising a mixture of carrier ampholytes, strong electrolyte auxiliary agents, weak electrolyte auxiliary agents, and ampholytic auxiliary agents to a second amount and effecting a second isoelectric focusing of the ampholytic analyte ([0087], [0090], [0092] – [0093]); and a means of detecting at a desired second focusing position in the separation compartment the ampholytic analyte at its increased concentration over that provided by isoelectric focusing without the use of any auxiliary compartment and auxiliary agent ([0130]).

Regarding claims 25 – 28, Vigh ('465) discloses the apparatus according to claim 22, wherein the separation compartment is part of an imaging capillary isoelectric focusing system ([0130]).

Regarding claims 29 – 30, Vigh ('465) discloses the apparatus according to claim 22, additionally including an anti-convective, ion-permeable membrane (30, 32) between the auxiliary compartment and the adjacent electrode compartment that substantially eliminates convective mixing between the contents of the auxiliary compartment and the adjacent electrode compartment ([102], [106] – [107], [0115] – [0117]).

Regarding claims 31 and 33, Vigh ('465) discloses the apparatus according to claim 22, wherein the means of detection is an imaging light absorbance detector ([0130]).

Regarding claim 35, Vigh ('465) discloses a method of improving a concentration detection limit for an ampholytic analyte in an isoelectric focusing system ([0057]), comprising the steps of: providing an isoelectric focusing system (see fig. 2) including a separation compartment (26, 28) disposed between an anode compartment (22, 24) having an anode (88a, 88b) therein and a cathode compartment (24, 22) having a cathode (88b, 88a) therein; providing a solution containing an ampholytic analyte ([0002], [0129]) and a mixture of carrier ampholytes ([0130]); mixing at least one auxiliary agent with the solution containing the ampholytic analyte and mixture of carrier ampholytes ([0090], [0092], [0130]); filling the anode compartment with an acidic solution and the cathode compartment with a basic solution ([0129]); filling the separation compartment with the solution containing the ampholytic analyte, mixture of carrier ampholytes, and at least one auxiliary agent ([0129]); applying a potential between the anode located in the anode compartment and the cathode located in the cathode compartment ([0098] – [0099] and [0129]) to effect an isoelectric focusing of the ampholytic analyte in the separation compartment ([0037], [0099]); and detecting the focused ampholytic analyte in the separation compartment at its increased concentration over that provided by isoelectric focusing without the use of the at least one auxiliary agent ([0130]).

Regarding claim 36, Vigh ('465) discloses the method according to claim 35, additionally including the step of adding at least one auxiliary compartment (28, 26) disposed between at least one of the anode compartment (22, 24) and the separation

compartment (26, 28) and the cathode compartment (24, 22) and the separation compartment (26, 28), and filling, along with the separation compartment, the at least one auxiliary compartment with the solution containing the ampholytic analyte and mixture of carrier ampholytes ([0089] – [0093], [0129] – [0130]).

Regarding claim 37, Vigh ('465) discloses a method of improving a concentration detection limit for an ampholytic analyte in an isoelectric focusing system ([0057]), comprising the steps of: providing an isoelectric focusing system (see fig. 2) including a separation compartment (26, 28) disposed between an anode compartment (22, 24) having an anode (88a, 88b) therein and a cathode compartment (24, 22) having a cathode (88b, 88a) therein; providing a solution containing an ampholytic analyte ([0002], [0129]) and a mixture of carrier ampholytes ([0130]); providing at least one auxiliary compartment (28, 26) disposed between at least one of the anode compartment and the separation compartment and the cathode compartment and the separation compartment (see fig. 1); filling the anode compartment with an acidic solution and the cathode compartment with a basic solution ([0129]); filling the separation compartment and the, at least one auxiliary compartment with the solution containing the ampholytic analyte and mixture of carrier ampholytes ([0129]); applying a potential between the anode located in the anode compartment and the cathode located in the cathode compartment ([0098] – [0099] and [0129]) to effect an isoelectric focusing of the ampholytic analyte in the separation compartment ([0037], [0099]); and detecting the focused ampholytic analyte in the separation compartment at its increased

concentration over that provided by isoelectric focusing without the use of the at least one auxiliary compartment ([0130]).

13. Claims 1, 7 – 24, 27, 29 – 30 and 35 – 37 are rejected under 35 U.S.C. 102(a) as being anticipated by Speicher et al. (US 6, 638, 408).

Regarding claim 1, Speicher ('408) discloses a method of improving a concentration detection limit for an ampholytic analyte in an isoelectric focusing system (column 9, lines 29 – 39) comprising the steps of: providing an isoelectric focusing system (such as one in figs. 1, 8 and 9) having a separation compartment (190) disposed between an anode compartment (170) and a cathode compartment (210); providing a solution containing an ampholytic analyte and a mixture of carrier ampholytes (column 8, lines 27 – 36 and column 12, lines 11 – 14); providing at least one of the options selected from the group consisting of option one and option two, wherein option one uses one or more auxiliary compartments (180, 200) disposed between at least one of the anode compartment and the separation compartment or the cathode compartment and the separation compartment (see fig. 1), and option two uses one or more auxiliary agents mixed with the solution containing the ampholytic sample component; filling the anode compartment with an acidic solution and the cathode compartment with a basic solution (column 5, lines 7 – 35 and column 16, lines 31 – 34); filling the other compartments with the solution containing the ampholytic analyte; applying a potential between an anode (+) located in the anode compartment and a

cathode (-) located in the cathode compartment and effecting an isoelectric focusing of the ampholytic analyte into the separation compartment (column 8, lines 27 – 36 , column 16, lines 29 – 31 and column 12, lines 11 – 14); and detecting the focused ampholytic analyte in the separation compartment at its increased concentration over that provided by isoelectric focusing without the use of option one or option two (column 9, lines 51 – 54 and lines 29 – 39)

Regarding claims 7 and 8, Speicher ('408) discloses the method according to claim 1, wherein the auxiliary compartment and the adjacent electrode compartment are separated by an anti-convective, ion-permeable membrane (130, 160) that substantially eliminates convective mixing between the contents of the auxiliary compartment and the adjacent electrode compartment (column 5, lines 7 – 17).

Regarding claims 9 – 19, Speicher ('408) discloses the method according to claim 1, option one, which uses one or more auxiliary compartments. Claim 1 requires only one of the alternatives, option one or option two. Because Speicher ('408) discloses option one and claims 9 – 19 further limit option 2, claims 9 – 19 are also anticipated by Speicher ('408).

Regarding claim 20, Speicher ('408) discloses the method according to claim 1, wherein one or more solubilizer selected from a group consisting of non-electrolytes and zwitterions is additionally added to the sample solution to increase the solubility of the ampholytic analyte (column 8, lines 27 – 31, column 12, lines 11 – 14).

Regarding claim 21, Speicher ('408) discloses the method according to claim 1, wherein one or more complexing agent selected from group consisting of non-electrolytes and zwitterions is additionally added to the sample solution to improve the isoelectric focusing separation of the ampholytic analyte (column 7, line 66 – column 8, line 6, column 8, lines 27 – 31, column 12, lines 11 – 14 and column 11, lines 5 – 63).

Regarding claim 22, Speicher ('408) discloses an apparatus (see figs. 1, 8 and 9) comprising: a separation compartment (190) disposed between an anode compartment (170) and a cathode compartment (210); an anode (+) disposed in the anode compartment and a cathode (-) disposed in the cathode compartment; one or more auxiliary compartments (180, 200) disposed between the anode compartment and the separation compartment or the cathode compartment and the separation compartment; a means (column 5, lines 7 – 17) of filling the anode compartment with an acidic solution and the cathode compartment with a basic solution; a means (230) of filling the rest of the compartments with a solution that contains an ampholytic analyte, and one or more components selected from a group comprising a mixture of carrier ampholytes, strong electrolyte auxiliary agents, weak electrolyte auxiliary agents, and ampholytic auxiliary agents (column 7, lines 18 – 23); a means of applying a separation potential to the anode and the cathode and effecting an isoelectric focusing of the ampholytic analyte into the separation compartment (column 7, lines 28 – 39); and a means of detecting the focused ampholytic analyte in the separation compartment at its increased

concentration over that provided by isoelectric focusing without the use of any auxiliary compartment and auxiliary agent (column 9, lines 51 – 54 and lines 29 – 39).

Regarding claim 23, Speicher ('408) discloses an apparatus (see figs. 1, 8 and 9) comprising: a separation compartment (190) disposed between an anode compartment (170) and a cathode compartment (210); an anode (+) disposed in the anode compartment and a cathode (-) disposed in the cathode compartment; one or more auxiliary compartments (180, 200) disposed between the anode compartment and the separation compartment or the cathode compartment and the separation compartment; a means (column 5, lines 7 – 17) of filling the anode compartment with an acidic solution and the cathode compartment with a basic solution; a means (230) of filling the rest of the compartments with a solution that contains an ampholytic analyte present in a salt-laden sample (column 12, lines 18 – 23) and a first amount of one or more components selected from a group comprising a mixture of carrier ampholytes, strong electrolyte auxiliary agents, weak electrolyte auxiliary agents, and ampholytic auxiliary agents (column 7, lines 18 – 23); a means of applying a separation potential to the anode and the cathode and effecting a first isoelectric focusing of the ampholytic analyte into the separation compartment (column 7, lines 28 – 39); a means of detecting at a first focusing position in the separation compartment the focused ampholytic analyte at its increased concentration (column 9, lines 51 – 54 and lines 29 – 39); a means of adjusting in the ampholytic analyte containing solution the first amount of the one or more components selected from the group comprising a mixture of carrier

ampholytes, strong electrolyte auxiliary agents, weak electrolyte auxiliary agents, and ampholytic auxiliary agents to a second amount and effecting a second isoelectric focusing of the ampholytic analyte (column 9, lines 7 – 32 and column 7, lines 28 – 39); and a means of detecting at a desired second focusing position in the separation compartment the ampholytic analyte at its increased concentration over that provided by isoelectric focusing without the use of any auxiliary compartment and auxiliary agent (column 9, lines 51 – 54 and lines 29 – 39).

Regarding claim 24, Speicher ('408) discloses the apparatus according to claim 22, wherein there is one auxiliary compartment (180) disposed between the anode compartment (170) and the separation compartment (190) and another auxiliary compartment (200) disposed between the separation compartment (190) and the cathode compartment (210).

Regarding claim 27, Speicher ('408) discloses the apparatus according to claim 22, wherein the separation compartment is part of an isoelectric focusing system (see figs. 1, 8 and 9 and column 4, lines 46 – 51).

Regarding claim 29, Speicher ('408) discloses the apparatus according to claim 22, additionally including an anti-convective, ion-permeable barrier (130, 160) between the auxiliary compartment and the adjacent electrode compartment that substantially eliminates convective mixing between the contents of the auxiliary compartment and the adjacent electrode compartment (column 5, lines 7 – 17).

Regarding claim 30, Speicher ('408) discloses the apparatus according to claim 22, additionally including an anti-convective, ion-permeable membrane (130, 160) between the auxiliary compartment and the adjacent electrode compartment that substantially eliminates convective mixing between the contents of the auxiliary compartment and the adjacent electrode compartment (column 5, lines 7 – 17).

Regarding claim 35, Speicher ('408) discloses a method of improving a concentration detection limit for an ampholytic analyte in an isoelectric focusing system (column 17, lines 6 – 25), comprising the steps of: providing an isoelectric focusing system (such as in figs. 1, 8 and 9) including a separation compartment (190) disposed between an anode compartment (170) having an anode (+) therein and a cathode compartment (210) having a cathode (-) therein; providing a solution containing an ampholytic analyte and a mixture of carrier ampholytes (column 8, lines 27 – 36 and column 12, lines 11 – 14); mixing at least one auxiliary agent with the solution containing the ampholytic analyte and mixture of carrier ampholytes (column 8, lines 27 – 31 and column 12, lines 11 – 14); filling the anode compartment with an acidic solution and the cathode compartment with a basic solution (column 5, lines 7 – 35 and column 16, lines 31 – 34); filling the separation compartment with the solution containing the ampholytic analyte, mixture of carrier ampholytes, and at least one auxiliary agent (column 8, lines 27 – 36 , column 16, lines 29 – 31 and column 12, lines 11 – 14); applying a potential between the anode located in the anode compartment and the cathode located in the cathode compartment to effect an isoelectric focusing of the

ampholytic analyte in the separation compartment (column 7, lines 40 – 53); and detecting the focused ampholytic analyte in the separation compartment at its increased concentration over that provided by isoelectric focusing without the use of the at least one auxiliary compartment (column 9, lines 51 – 54 and lines 29 – 39).

Regarding claim 36, Speicher ('408) discloses the method according to claim 35, additionally including the step of adding at least one auxiliary compartment (180, 200) disposed between at least one of the anode compartment and the separation compartment and the cathode compartment and the separation compartment (see figs. 1, 8 and 9), and filling, along with the separation compartment, the at least one auxiliary compartment with the solution containing the ampholytic analyte and mixture of carrier ampholytes (column 8, lines 27 – 36 , column 16, lines 29 – 31 and column 12, lines 11 – 14).

Regarding claim 37, Speicher ('408) discloses a method of improving a concentration detection limit for an ampholytic analyte in an isoelectric focusing system (column 17, lines 6 – 25), comprising the steps of: providing an isoelectric focusing system (such as in figs. 1, 8 and 9) including a separation compartment (190) disposed between an anode compartment (170) having an anode (+) therein and a cathode compartment (210) having a cathode (-) therein; providing a solution containing an ampholytic analyte and a mixture of carrier ampholytes (column 8, lines 27 – 36 and column 12, lines 11 – 14); providing at least one auxiliary compartment (180, 200)

disposed between at least one of the anode compartment and the separation compartment and the cathode compartment and the separation compartment (see figs. 1, 8 and 9); filling the anode compartment with an acidic solution and the cathode compartment with a basic solution (column 5, lines 7 – 35 and column 16, lines 31 – 34); filling the separation compartment and the, at least one auxiliary compartment with the solution containing the ampholytic analyte and mixture of carrier ampholytes (column 8, lines 27 – 36 , column 16, lines 29 – 31 and column 12, lines 11 – 14); applying a potential between the anode located in the anode compartment and the cathode located in the cathode compartment to effect an isoelectric focusing of the ampholytic analyte in the separation compartment (column 7, lines 40 – 53); and detecting the focused ampholytic analyte in the separation compartment at its increased concentration over that provided by isoelectric focusing without the use of the at least one auxiliary compartment (column 9, lines 51 – 54 and lines 29 – 39).

14. Claims 1 – 4, 7 – 15, 17, 20 – 23, 25 – 31, 33, 35 – 37 are rejected under 35 U.S.C. 102(a) as being anticipated by Shave et al. ("Preparative-scale, recirculating, pH-biased binary isoelectric trapping separations", Electrophoresis, Volume 25, (2004), pages 381-387, published online 19 January 2004).

Regarding claim 1, Shave discloses a method of improving a concentration detection limit for an ampholytic analyte in an isoelectric focusing system (see "4 Concluding Remarks" section on page 386) comprising the steps of: providing an isoelectric focusing system having a separation compartment disposed between an

anode compartment and a cathode compartment (see description of BF200IET system in paragraph bridging pages 381 and 382); providing a solution containing an ampholytic analyte and a mixture of carrier ampholytes (see section "2 Materials and methods" on pages 382 – 383); providing at least one of the options selected from the group consisting of option one and option two, wherein option one uses one or more auxiliary compartments disposed between at least one of the anode compartment and the separation compartment or the cathode compartment and the separation compartment, and option two uses one or more auxiliary agents mixed with the solution containing the ampholytic sample component (page 382, paragraph bridging left and right columns); filling the anode compartment with an acidic solution and the cathode compartment with a basic solution (page 384, section "3.2 Preparative-scale binary IET separations of chicken egg white with CAR as the pH-biaser"); filling the other compartments with the solution containing the ampholytic analyte (page 384, section "3.2 Preparative-scale binary IET separations of chicken egg white with CAR as the pH-biaser"); applying a potential between an anode located in the anode compartment and a cathode located in the cathode compartment and effecting an isoelectric focusing of the ampholytic analyte into the separation compartment (paragraph bridging pages 384 and 385); and detecting the focused ampholytic analyte in the separation compartment at its increased concentration over that provided by isoelectric focusing without the use of option one or option two (page 383, section "2.3 Analysis of the collected samples").

Regarding claim 2, Shave discloses a method of improving a concentration detection limit for an ampholytic analyte in an isoelectric focusing system and eliminating a deformation of a pH gradient in the isoelectric focusing analysis of a salt-laden sample containing an ampholytic analyte (see "4 Concluding Remarks" section on page 386) comprising the steps of: providing an isoelectric focusing system having a separation compartment disposed between an anode compartment and a cathode compartment (see description of BF200IET system in paragraph bridging pages 381 and 382); providing one or more auxiliary compartments disposed between at least one of the anode compartment and the separation compartment or the cathode compartment and the separation compartment (see description of BF200IET system in paragraph bridging pages 381 and 382); adding a mixture of carrier ampholytes and a first amount of one or more auxiliary agents to the salt-laden sample solution containing the ampholytic analyte (see section "2 Materials and methods" on pages 382 – 383); filling the anode compartment with an acidic solution and the cathode compartment with a basic solution (page 384, section "3.2 Preparative-scale binary IET separations of chicken egg white with CAR as the pH-biaser"); filling the other compartments with the solution containing the ampholytic analyte (page 384, section "3.2 Preparative-scale binary IET separations of chicken egg white with CAR as the pH-biaser"); applying a potential between an anode located in the anode compartment and a cathode located in the cathode compartment and effecting a first isoelectric focusing of the ampholytic analyte into the separation compartment (paragraph bridging pages 384 and 385); detecting at a first focusing position in the separation compartment the focused

ampholytic analyte (page 383, section "2.3 Analysis of the collected samples"); adjusting the first amount of the one or more auxiliary agents added to the salt-laden sample solution containing the ampholytic analyte to a second amount and effecting a second isoelectric focusing of the ampholytic analyte into the separation compartment (page 386, left column, 2nd full paragraph); and detecting at a desired second focusing position in the separation compartment the focused ampholytic analyte at its increased concentration over that provided in an isoelectric focusing without the use of an auxiliary compartment or an auxiliary agent (page 383, section "2.3 Analysis of the collected samples").

Regarding claims 3 and 4, Shave discloses the method according to claim 1, wherein the isoelectric focusing system is an imaging capillary isoelectric focusing system (page 383, section "2.3 Analysis of the collected samples").

Regarding claims 7 and 8, Shave discloses the method according to claim 1, wherein the auxiliary compartment and the adjacent electrode compartment are separated by an anti-convective, ion-permeable membrane that substantially eliminates convective mixing between the contents of the auxiliary compartment and the adjacent electrode compartment (see description of BF200IET system in paragraph bridging pages 381 and 382).

Regarding claims 9 – 14, Shave discloses the method according to claim 1, wherein the multiple auxiliary agents used are selected to belong to the same or different subgroups of strong electrolytes, weak electrolytes, and ampholytes and

wherein the difference between the pI value of the ampholytic auxiliary agent and its nearest pKa value is less than 0.75 (page 382, section "2.1 Chemicals", page 384, paragraph bridging left and right columns, pages 383 – 384, section "3.1 Model considerations").

Regarding claim 15, Shave discloses the method according to claim 1, wherein one or more of the auxiliary agents absorb light at a selected detection wavelength (see figs. 3 and 4 and page 385, full paragraph on left column).

Regarding claim 17, Shave discloses the method according to claim 1, wherein one or more of the ampholytic auxiliary agents are selected from a group consisting of cysteic acid, N,N-dimethyliminodiacetic acid, N-methylaminodiacetic acid, iminodiacetic acid, benzeneiminodiacetic acid, aspartic acid, glutamic acid, ornithine, lysine, terbutaline, tyramine, arginine (page 382, paragraph bridging left and right columns, section "2.1 Chemicals").

Regarding claims 20 and 21, Shave discloses the method according to claim 1, wherein one or more solubilizer or complexing agent selected from a group consisting of non-electrolytes and zwitterions is additionally added to the sample solution to increase the solubility of the ampholytic analyte or to improve the isoelectric focusing separation of the ampholytic analyte (page 382, paragraph bridging left and right columns, section "2.1 Chemicals").

Regarding claim 22, Shave discloses an apparatus comprising: a separation compartment disposed between an anode compartment and a cathode compartment;

an anode disposed in the anode compartment and a cathode disposed in the cathode compartment; one or more auxiliary compartments disposed between the anode compartment and the separation compartment or the cathode compartment and the separation compartment (see description of BF200IET system in paragraph bridging pages 381 and 382); a means of filling the anode compartment with an acidic solution and the cathode compartment with a basic solution (paragraph bridging pages 382 – 383); a means of filling the rest of the compartments with a solution that contains an ampholytic analyte, and one or more components selected from a group comprising a mixture of carrier ampholytes, strong electrolyte auxiliary agents, weak electrolyte auxiliary agents, and ampholytic auxiliary agents (paragraph bridging pages 382 – 383); a means of applying a separation potential to the anode and the cathode and effecting an isoelectric focusing of the ampholytic analyte into the separation compartment (paragraph bridging pages 382 – 383); and a means of detecting the focused ampholytic analyte in the separation compartment at its increased concentration over that provided by isoelectric focusing without the use of any auxiliary compartment and auxiliary agent (page 383, section "2.3 Analysis of the collected samples").

Regarding claim 23, Shave discloses an apparatus comprising: a separation compartment disposed between an anode compartment and a cathode compartment; an anode disposed in the anode compartment and a cathode disposed in the cathode compartment; one or more auxiliary compartments disposed between the anode compartment and the separation compartment or the cathode compartment and the

separation compartment (see description of BF200IET system in paragraph bridging pages 381 and 382); a means of filling the anode compartment with an acidic solution and the cathode compartment with a basic solution (paragraph bridging pages 382 – 383); a means of filling the rest of the compartments with a solution that contains an ampholytic analyte present in a salt-laden sample and a first amount of one or more components selected from a group comprising a mixture of carrier ampholytes, strong electrolyte auxiliary agents, weak electrolyte auxiliary agents, and ampholytic auxiliary agents (paragraph bridging pages 382 – 383); a means of applying a separation potential to the anode and the cathode and effecting a first isoelectric focusing of the ampholytic analyte into the separation compartment (paragraph bridging pages 382 – 383); a means of detecting at a first focusing position in the separation compartment the focused ampholytic analyte at its increased concentration (page 383, section "2.3 Analysis of the collected samples"); a means of adjusting in the ampholytic analyte containing solution the first amount of the one or more components selected from the group comprising a mixture of carrier ampholytes, strong electrolyte auxiliary agents, weak electrolyte auxiliary agents, and ampholytic auxiliary agents to a second amount and effecting a second isoelectric focusing of the ampholytic analyte (page 386, left column, 2nd full paragraph); and a means of detecting at a desired second focusing position in the separation compartment the ampholytic analyte at its increased concentration over that provided by isoelectric focusing without the use of any auxiliary compartment and auxiliary agent (page 383, section "2.3 Analysis of the collected samples").

Regarding claims 25 – 28, Shave discloses the apparatus according to claim 22, wherein the separation compartment is part of an imaging capillary isoelectric focusing system (page 383, section "2.3 Analysis of the collected samples").

Regarding claims 29 – 30, Shave discloses the apparatus according to claim 22, additionally including an anti-convective, ion-permeable membrane between the auxiliary compartment and the adjacent electrode compartment that substantially eliminates convective mixing between the contents of the auxiliary compartment and the adjacent electrode compartment.

Regarding claims 31 and 33, Shave discloses the apparatus according to claim 22, wherein the means of detection is an imaging light absorbance detector (page 383, section "2.3 Analysis of the collected samples", see figs. 3 and 4 and page 385, full paragraph on left column).

Regarding claim 35, Shave discloses a method of improving a concentration detection limit for an ampholytic analyte in an isoelectric focusing system (see "4 Concluding Remarks" section on page 386), comprising the steps of: providing an isoelectric focusing system including a separation compartment disposed between an anode compartment having an anode therein and a cathode compartment having a cathode therein (see description of BF200IET system in paragraph bridging pages 381 and 382); providing a solution containing an ampholytic analyte and a mixture of carrier ampholytes (page 383, section "2.3 Analysis of the collected samples"); mixing at least

one auxiliary agent with the solution containing the ampholytic analyte and mixture of carrier ampholytes (page 384, paragraph bridging left and right columns); filling the anode compartment with an acidic solution and the cathode compartment with a basic solution (page 384, section "3.2 Preparative-scale binary IET separations of chicken egg white with CAR as the pH-biaser"); filling the separation compartment with the solution containing the ampholytic analyte, mixture of carrier ampholytes, and at least one auxiliary agent (page 384, section "3.2 Preparative-scale binary IET separations of chicken egg white with CAR as the pH-biaser"); applying a potential between the anode located in the anode compartment and the cathode located in the cathode compartment to effect an isoelectric focusing of the ampholytic analyte in the separation compartment (paragraph bridging pages 384 and 385); and detecting the focused ampholytic analyte in the separation compartment at its increased concentration over that provided by isoelectric focusing without the use of the at least one auxiliary agent (page 383, section "2.3 Analysis of the collected samples").

Regarding claim 36, Shave discloses the method according to claim 35, additionally including the step of adding at least one auxiliary compartment disposed between at least one of the anode compartment and the separation compartment and the cathode compartment and the separation compartment (see description of BF200IET system in paragraph bridging pages 381 and 382), and filling, along with the separation compartment, the at least one auxiliary compartment with the solution containing the ampholytic analyte and mixture of carrier ampholytes (page 384, section

"3.2 Preparative-scale binary IET separations of chicken egg white with CAR as the pH-biaser").

Regarding claim 37, Shave discloses a method of improving a concentration detection limit for an ampholytic analyte in an isoelectric focusing system (see "4 Concluding Remarks" section on page 386), comprising the steps of: providing an isoelectric focusing system including a separation compartment disposed between an anode compartment having an anode therein and a cathode compartment having a cathode therein (see description of BF200IET system in paragraph bridging pages 381 and 382); providing a solution containing an ampholytic analyte and a mixture of carrier ampholytes (page 383, section "2.3 Analysis of the collected samples"); providing at least one auxiliary compartment disposed between at least one of the anode compartment and the separation compartment and the cathode compartment and the separation compartment (see description of BF200IET system in paragraph bridging pages 381 and 382); filling the anode compartment with an acidic solution and the cathode compartment with a basic solution (page 384, section "3.2 Preparative-scale binary IET separations of chicken egg white with CAR as the pH-biaser"); filling the separation compartment and the, at least one auxiliary compartment with the solution containing the ampholytic analyte and mixture of carrier ampholytes (page 384, section "3.2 Preparative-scale binary IET separations of chicken egg white with CAR as the pH-biaser"); applying a potential between the anode located in the anode compartment and the cathode located in the cathode compartment to effect an isoelectric focusing of the

ampholytic analyte in the separation compartment (paragraph bridging pages 384 and 385); and detecting the focused ampholytic analyte in the separation compartment at its increased concentration over that provided by isoelectric focusing without the use of the at least one auxiliary compartment (page 383, section "2.3 Analysis of the collected samples").

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. Claims 2 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vigh et al. (US 2002/0043465).

Regarding claim 2, Vigh ('465) discloses a method of improving a concentration detection limit for an ampholytic analyte in an isoelectric focusing system ([0057]) and eliminating a deformation of a pH gradient in the isoelectric focusing analysis of a salt-laden sample containing an ampholytic analyte ([0003], [0039] – [0040]) comprising the steps of: providing an isoelectric focusing system (see fig. 2) having a separation compartment (26, 28) disposed between an anode compartment (22, 24) and a cathode compartment (24, 22); providing one or more auxiliary compartments (28, 26) disposed between at least one of the anode compartment (22, 24) and the separation compartment (26, 28) or the cathode compartment (24, 22) and the separation compartment (26, 28); adding a mixture of carrier ampholytes ([0130]) and a first amount of one or more auxiliary agents ([0090], [0092], [0130]) to the salt-laden sample solution containing the ampholytic analyte ([0090], [0092], [0129], [0040]); filling the anode compartment with an acidic solution and the cathode compartment with a basic solution ([0130]); filling the other compartments with the solution containing the ampholytic analyte ([0129]); applying a potential between an anode (88a, 88b) located in the anode compartment and a cathode (88b, 88a) located in the cathode compartment ([0098] – [0099] and [0129]) and effecting a first isoelectric focusing of the ampholytic analyte into the separation compartment ([0037] and [0099]); detecting at a first focusing position in the separation compartment the focused ampholytic analyte ([0130]); and detecting at a desired second focusing position in the separation compartment the focused ampholytic analyte at its increased concentration over that provided in an isoelectric focusing without the use of an auxiliary compartment or an

auxiliary agent ([0130]). Vigh ('465) does not explicitly disclose adjusting the first amount of the one or more auxiliary agents added to the salt-laden sample solution containing the ampholytic analyte to a second amount and effecting a second isoelectric focusing of the ampholytic analyte into the separation compartment. However, Vigh ('465) discloses adjusting the flow rate of the analyte and electrolytes depending on the process, the component or components to be transferred, efficiency of transfer, and coupling of the process with other, preceding or following processes ([0093]) which would have suggested the adjusting step ([0087], [0090], [0092] – [0093]) to one of ordinary skill in the art.

Vigh ('465) discloses the apparatus as discussed with regards to claim 22. Regarding claim 24, Vigh ('465) discloses one auxiliary compartment (28, 26) between the separation compartment (26, 28) and one of the anode and cathode compartments (22, 24). Vigh ('465) does not explicitly disclose another auxiliary compartment. See *In re Harza*, 274 F.2d 669, 124 USPQ 378 (CCPA 1960) regarding the obviousness of duplication of parts.

18. Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vigh et al. (US 2002/0043465) in view of Hofmann et al. ("Adaptation of Capillary Isoelectric Focusing to Microchannels on a Glass Chip", Analytical Chemistry, Vol. 71, No. 3, February 1, 1999, pages 678 – 686).

Vigh ('465) discloses the method as discussed with regards to claim 1. Regarding claims 5 and 6, Vigh ('465) does not explicitly disclose the isoelectric focusing system to be a chip-based isolectric focusing system.

Hofmann teaches a chip-based isolectric focusing system (see fig. 1 and abstract).

It would have been obvious to one of ordinary skill in the art to have adapted the capillary imaging isolectric focusing system of Vigh ('465) to a chip-based system as taught by Hofmann because it provides the benefit of miniaturization which translates to low cost, speed and portability as explained by Hofmann (page 679, 2nd full paragraph on left hand column).

19. Claims 32 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vigh et al. (US 2002/0043465) in view of Wu et al. (US 5,985,121).

Vigh ('465) discloses the apparatus as discussed with regards to claim 22 above. Regarding claims 32 and 34, Vigh ('465) discloses the means of detection is an imaging detector ([0130]). Vigh ('465) does not expressly disclose the detector to be a fluorescence – based detector.

Wu ('121) teaches an apparatus for isolectric focusing with a universal refractive index gradient imaging detector, an optical absorption imaging detector, and a fluorescence imaging detector (column 2, lines 57 – 62).

It would have been obvious to one of ordinary skill in the art to have included the any one of the detectors taught by Wu ('121) in the apparatus of Vigh ('465) because Wu ('121) explains that these detectors overcome problems arising from mobilization process associated with conventional on-column detectors through the use of their new on-line, real-time imaging detector (column 2, lines 54 – 57).

20. Claims 3 – 4, 25 – 26 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Speicher et al. (US 6, 638, 408) in view of Pawliszyn (US 5,784,154).

Speicher ('408) discloses the method as discussed with regards to claim 1 above. Regarding claims 3 and 4, Speicher ('408) discloses a chamber (100) wherein isoelectric focusing occurs. Speicher ('408) does not expressly disclose the isoelectric focusing system is a capillary isoelectric focusing system.

Pawliszyn ('154) teaches an imaging capillary isoelectric focusing system as an improvement over isoelectric focusing performed in chambers (column 2, lines 27 – 32 and column 18, lines 48 – 51).

It would have been obvious to one of ordinary skill in the art to have modified the isoelectric focusing system of Speicher ('408) to an imaging capillary isoelectric focusing system as taught by Pawliszyn ('154) because as Pawliszyn ('154) explains it has the benefit of efficient dissipation of Joule heat, eliminates convection effects which occur in large chambers and enables highly efficient separations (column 2, lines 27 – 32).

Speicher ('408) discloses the apparatus as discussed with regards to claim 22 above. Regarding claims 25 – 26 and 28, Speicher ('408) discloses a chamber (100) wherein isoelectric focusing occurs. Speicher ('408) does not expressly disclose the isoelectric focusing system is a capillary isoelectric focusing system or an imaging isoelectric focusing system.

Pawliszyn ('154) teaches an imaging capillary isoelectric focusing system as an improvement over isoelectric focusing performed in chambers (column 2, lines 27 – 32 and column 18, lines 48 – 51).

It would have been obvious to one of ordinary skill in the art to have modified the isoelectric focusing system of Speicher ('408) to an imaging capillary isoelectric focusing system as taught by Pawliszyn ('154) because as Pawliszyn ('154) explains it has the benefit of efficient dissipation of Joule heat, eliminates convection effects which occur in large chambers and enables highly efficient separations (column 2, lines 27 – 32).

21. Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Speicher et al. (US 6, 638, 408) in view of Pawliszyn (US 5,784,154) and Hofmann et al. ("Adaptation of Capillary Isoelectric Focusing to Microchannels on a Glass Chip", Analytical Chemistry, Vol. 71, No. 3, February 1, 1999, pages 678 – 686).

Speicher ('408) discloses the method as discussed with regards to claim 1 above. Regarding claims 5 and 6, Speicher ('408) discloses a chamber (100) wherein isoelectric focusing occurs. Speicher ('408) does not expressly disclose the isoelectric focusing system is a chip-based isoelectric focusing system.

Pawliszyn ('154) teaches an imaging capillary isoelectric focusing system as an improvement over isoelectric focusing performed in chambers (column 2, lines 27 – 32 and column 18, lines 48 – 51).

It would have been obvious to one of ordinary skill in the art to have modified the isoelectric focusing system of Speicher ('408) to an imaging capillary isoelectric focusing system as taught by Pawliszyn ('154) because as Pawliszyn ('154) explains it has the benefit of efficient dissipation of Joule heat, eliminates convection effects which occur in large chambers and enables highly efficient separations (column 2, lines 27 – 32).

Pawliszyn ('154) does not explicitly disclose the imaging capillary isoelectric system to be a chip-based system.

Hofmann teaches a chip-based isolectric focusing system (see fig. 1 and abstract).

It would have been obvious to one of ordinary skill in the art to have adapted the capillary imaging isolectric focusing system of Speicher ('408) in view of Pawliszyn ('154) to a chip-based system as taught by Hofmann because it provides the benefit of miniaturization which translates to low cost, speed and portability as explained by Hofmann (page 679, 2nd full paragraph on left hand column).

22. Claims 31 – 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Speicher et al. (US 6, 638, 408) in view of Wu et al. (US 5,985,121).

Speicher ('408) discloses the apparatus as discussed with regards to claim 22 above. Regarding claims 31 – 34, Speicher ('408) discloses a means of detection (column 9, lines 51 – 54). Speicher ('408) does not explicitly disclose the means of detection is a light absorbance or fluorescence detector.

Wu ('121) teaches an apparatus for isolectric focusing with a universal refractive index gradient imaging detector, an optical absorption imaging detector, and a fluorescence imaging detector (column 2, lines 57 – 62).

It would have been obvious to one of ordinary skill in the art to have included the any one of the detectors taught by Wu ('121) in the apparatus of Speicher ('408) because Wu ('121) explains that these detectors overcome problems arising from mobilization process associated with conventional on-column detectors through the use of their new on-line, real-time imaging detector (column 2, lines 54 – 57).

23. Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shave et al. ("Preparative-scale, recirculating, pH-biased binary isoelectric trapping separations", Electrophoresis, Volume 25, (2004), pages 381-387, published online 19 January 2004) in view of Hofmann et al. ("Adaptation of Capillary Isoelectric Focusing to

Microchannels on a Glass Chip", Analytical Chemistry, Vol. 71, No. 3, February 1, 1999, pages 678 – 686).

Shave discloses the method as discussed with regards to claim 1 above. Regarding claims 5 and 6, Shave does not explicitly disclose the isoelectric focusing system is a chip-based isoelectric focusing system.

Hofmann teaches a chip-based isolectric focusing system (see fig. 1 and abstract).

It would have been obvious to one of ordinary skill in the art to have adapted the capillary imaging isolectric focusing system of Shave to a chip-based system as taught by Hofmann because it provides the benefit of miniaturization which translates to low cost, speed and portability as explained by Hofmann (page 679, 2nd full paragraph on left hand column).

24. Claims 16, 32 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shave et al. ("Preparative-scale, recirculating, pH-biased binary isoelectric trapping separations", Electrophoresis, Volume 25, (2004), pages 381-387, published online 19 January 2004) in view of Wu et al. (US 5,985,121).

Shave discloses the method as discussed with regards to claim 1 above. Regarding claim 16, Shave does not explicitly disclose one or more of the auxiliary agents fluoresce.

Wu ('121) teaches an apparatus and a method of using the same for isolectric focusing with a universal refractive index gradient imaging detector, an optical absorption imaging detector, and a fluorescence imaging detector (column 2, lines 57 – 62).

It would have been obvious to one of ordinary skill in the art to have included the auxiliary agents that fluoresce to be detected by the fluorescence imaging detector taught by Wu ('121) in the method of Shave because Wu ('121) explains that these detectors overcome problems arising from mobilization process associated with conventional on-column detectors through the use of their new on-line, real-time imaging detector (column 2, lines 54 – 57).

Shave discloses the apparatus as discussed with regards to claim 22 above. Regarding claims 32 and 34, Shave does not explicitly disclose the means of detection is an imaging fluorescence detector.

Wu ('121) teaches an apparatus for isolectric focusing with a universal refractive index gradient imaging detector, an optical absorption imaging detector, and a fluorescence imaging detector (column 2, lines 57 – 62).

It would have been obvious to one of ordinary skill in the art to have included the any one of the detectors taught by Wu ('121) in the apparatus of Shave because Wu ('121) explains that these detectors overcome problems arising from mobilization process associated with conventional on-column detectors through the use of their new on-line, real-time imaging detector (column 2, lines 54 – 57).

25. Claims 18 – 19 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shave et al. ("Preparative-scale, recirculating, pH-biased binary isoelectric trapping separations", Electrophoresis, Volume 25, (2004), pages 381-387, published online 19 January 2004).

Shave discloses the method according to claim 1 as discussed above. Regarding claims 18 and 19, Shave does not explicitly disclose the auxiliary agents to be those recited in the claims. Shave however discloses characteristics of a suitable auxiliary agent including choosing an agent with appropriate pI relative to that of the analyte, solubility of the agent, etc. (page 382, paragraph bridging left and right columns, page 386, section "4 Concluding remarks") which would have suggested any one of the agents listed in claims 18 and 19 to one of ordinary skill in the art.

Shave discloses the apparatus as discussed with regards to claim 22 above. Regarding claim 24, Shave discloses one auxiliary compartment between the separation compartment and one of the anode and cathode compartments (see description of BF200IET system in paragraph bridging pages 381 and 382). Shave does not explicitly disclose another auxiliary compartment. See *In re Harza*, 274 F.2d 669, 124 USPQ 378 (CCPA 1960) regarding the obviousness of duplication of parts.

Conclusion

26. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Vigh (US 2002/0060154) discloses an isoelectric focusing system comprising multiple compartments separated by ion-permeable barriers.

Gillis (US 4,411,992) discloses addition of auxiliary agent (aspartic acid) to an ampholytic analyte (IL-2) in addition to carrier ampholytes in order to perform isoelectric focusing.

Hjertén et al. (US 5,464,517) discloses the use of several auxiliary agents such as lysine, aspartic acid, and iminodiacetic acid for use in isoelectric focusing system.

Liao et al. (5,766,435) discloses a method of concentrating samples in addition to desalting them in a pH gradient.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Surekha Vathyam whose telephone number is 571-272-2682. The examiner can normally be reached on 7:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam X. Nguyen can be reached on 571-272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SV/
3 September 2007

NAM NGUYEN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1700